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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MITCHELL, GREGORY W	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 10/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,427	THOR, KARL BRUCE	
	Examiner	Art Unit	
	Gregory W. Mitchell	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-42 and 51-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-42 and 51-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/08/05; 02/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the Remarks filed July 08, 2005. Claims 37-42 and 51-54 are pending and are examined herein. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

35 USC § 103 Rejection Maintained

Claims 37-42 and 51-54 stand rejected under 35 U.S.C. 103(a) as being unpatentable over McMahon et al. (*J. Urology*, 161, 1826-30) and Lane (*J. Psychopharmacology*, 11(1), 72-82) in view of Eli Lily (ZA 9300694) and Robertson et al. (USPN 5135947) for the reasons set forth in the Office Action dated March 10, 2005.

Applicant argues, "The combination of these references does not teach or suggest the claim element of as-needed administration. The Examiner addresses this deficiency by characterizing the claim element as mere optimization." This argument is not persuasive because Examiner has not addressed said element in such a manner. Examiner has relied on both McMahon et al. and Lane, both of whom teach the administration of SSRIs on an as-needed basis. It is the quantity of agent to be administered that Examiner has addressed as being mere optimization of the obvious invention and, thereby, itself obvious.

Applicant argues, "the [McMahon et al.] authors ***postulate*** 'serotonin re-uptake inhibitors should reduce sexual excitement and have a beneficial effect on premature ejaculation.' ... This statement by the authors is merely an initial observation from a rat

model that provided the impetus to pursue the small human trial described in McMahon and does not support the assertion that all SSRIs delay orgasm and have a beneficial effect on premature ejaculation in humans." This argument is not persuasive because the teaching of McMahon et al., as set forth above would, and/or the teaching of Lane, both in combination of Eli Lily and Roberson et al., lead one of ordinary skill in the art to select dapoxetine as an SSRI effective for the treatment of PE. In other words, the broad teaching of McMahon et al. and/or Lane would have led one of ordinary skill in the art to select dapoxetine and PE from the laundry list set forth by Eli Lily.

Applicant argues that in McMahon et al., "neither the design or the results of the studies would lead one of skill in the art to conclude that an SSRI could be used to treat PE patients on an as-needed basis." This argument is not persuasive because McMahon et al. clearly teaches the administration of the SSRIs therein on an "as needed" basis. See Abstract; p. 1827, Study 1; etc. When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980).

Applicant attempt to rebut the presumption of operability of McMahon et al. by arguing that "[t]he McMahon study did not use an appropriate number of men suffering with PE to address the study objective" and that "[t]he McMahon studies were single-blind studies". These arguments are not persuasive because Applicant's allegation that there are an insufficient number of test subjects does not address the presumption of

operability, but the "scientific validity". There is no reasons to assume that the standard required for one of ordinary skill in the art to accept the teachings of McMahon et al. as scientific certainty would be the same as the standard required for one of ordinary skill in the art to *presume* that the invention would *work*. It is further noted that there is no supporting documentation that McMahon's number of test subjects is insufficient for "scientific validity". Applicant's arguments regarding the single-blind studies are, likewise, unpersuasive. Applicant's argument that "on average, trials that have not used appropriate levels of blinding, such as McMahon, show larger treatment effects than blinded studies" is not sufficient to suggest to the skilled artisan that the teachings of McMahon should not be presumed enabled. First, it is noted that the teaching merely suggests that "on average" different levels of blinding produce different results. Second, there is only a suggestion that varying levels of blinding may lead to varying magnitudes of efficacy, not that the efficacy is, itself, questioned.

Applicant argues, "by [McMahon et al.'s] admission, [] there was no statistically superior increase in ejaculatory latency in the first week." This argument is not persuasive. First, the argument presupposes that the dosing during the first week of administration is, effectively, equivalent to a "priming dose". If such an argument were found to be persuasive, however, it would suggest that for a drug to be administered on an "as needed" basis in the absence of a priming dose, only the first administration of the drug would qualify as "as needed" in the absence of a priming dose. Second, the language of the disclosure clearly suggests that while a priming dose is preferred, it is not required. McMahon states that "paroxetine as needed was significantly better if

patients were initially treated with the drug daily." Such a suggestion would indicate to one of ordinary skill in the art that the effects of administration are the best when there is a priming dose, but that the administration of the drug in the absence of a priming dose would also be effective at achieving the desired results. Accordingly, Applicant's suggestion that Examiner is required to provide evidence that the data is of McMahon et al. for the first week is statistically significant when McMahon et al. says that it is not is not necessary. Furthermore, McMahon et al. clearly illustrates (Figure 1) that the mean ejaculatory interval was seen to increase after one week of administration of paroxetine in both Groups A and B by identical amounts and that the increase was more than that observed for placebo. The multiple of increase seen in Groups A and B (weeks 1 and 8, respectively) are comparable to those set forth in the instant specification (see, e.g., Table 9). Furthermore, it is noted that McMahon et al. does not state that the results of week 1 are *not* statistically superior. Accordingly, one of skill in the art would look to Fig. 1 to determine the results of week 1, wherein the skilled artisan would observe the increases in mean ejaculatory interval, as discussed above.

Applicant argues that because Lane states that "[t]he placebo-controlled studies with sertraline and paroxetine used high doses. The efficacy of the lower doses and different dosing regimens has yet to be fully explored" that Lane "questions the applicability of these two initial reports to the clinical use of sertraline and paroxetine themselves and certainly does not support the general efficacy of SSRIs in the treatment of PE." This argument is not persuasive because Lane does not suggest that the treatment does not work but merely that, as with all drugs, dosage optimization must

be determine and that once such a dosage optimization is determined that a cost/benefit analysis of the side effects and treatment benefits must be weighed.

Applicant argues that Lane's review of Swartz's "seemingly amazing results, that are inconsistent with any results available at that time, or that have been published subsequent to that report appear to have been an average of both daily and as-needed dosing." This argument is not persuasive because even if the results were indeed an average of both daily and as-needed dosing, such an averaging would not take away from the fact that Swartz via Lane clearly teaches administration on an as needed basis.

Applicant argues that the Swartz teaching that "the '26-hour elimination half life [of sertraline] allows considerable liberties in dosing schedules" indicates that the teaching is a "preliminary case report and, even in combination with the high dose studies of paroxetine and sertraline, one of skill in the art clearly would not regard this report as supporting that all SSRIs, administered in low doses on an as-needed basis prior to intercourse would be efficacious in treating PE." This argument is not persuasive because the teaching that there are considerable liberties in dosing schedules indicates merely that there are considerable liberties in dosing schedules or, in other words, that administration schedules may be adjusted to the particular needs of a patient. Furthermore, the Abstract of Lane clearly teaches that "selective serotonin reuptake inhibitors (SSRIs) are clearly associated with delayed ejaculation ...". This teaching, coupled with the other references, particularly Eli Lilly and Robertson et al., that it would have been obvious to treat PE with dapoxetine. Furthermore,

administration of SSRIs on an as-needed basis is disclosed as being efficacious by both Lane and McMahon et al., as discussed above.

Applicant argues, "While the prior art clearly indicates that SSRIs generally can cause sexual dysfunction and there was a suggestion that certain SSRIs might be useful for treating PE, there was no guidance that specific SSRIs were useful, nor any guidance in the art as to how to select SSRIs that would be useful." This argument is not persuasive because McMahon et al. and Lane teach the use of SSRIs for the treatment of PE on an as needed basis. Furthermore, the general teachings of McMahon et al. and Lane would lead one of ordinary skill in the art to Eli Lilly and Robertson et al. wherein the skilled artisan would find the teachings required to specifically select the specific SSRI dapoxetine for the treatment of PE.

Applicant argues, "Lilly merely includes dapoxetine in a laundry list of SSRIs and identifies a vast listing of conditions with which such compounds might be useful. Moreover, no data or experimental basis is provided that any of the compounds could be used with any of the conditions." Applicant further argues, "even if [Eli Lilly] is construed to effectively disclose the use of dapoxetine for premature ejaculation, there is no disclosure or suggestion of the use of dapoxetine on an as-needed basis or the characteristic that it is effective in the absence of priming doses." These argument are not persuasive because Eli Lilly is not used to reject the pending claims alone. The references of Lane, McMahon et al. and Robertson et al. would have provided the suggestion required for one of ordinary skill in the art to utilize the SSRIs of Eli Lilly specifically for the treatment of PE on an as-needed basis and McMahon et al. would

have indicated to the skilled artisan, for the reasons set forth above, that the administration of SSRIs on an as-needed basis is efficacious with or without priming doses. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Furthermore, the teaching of Eli Lilly is presumed to be enabled. When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory W Mitchell whose telephone number is 571-272-2907. The examiner can normally be reached on M-F, 8:30 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

gwm

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER